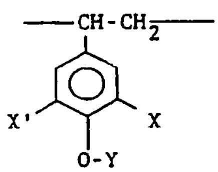
18

(12) UK Patent Application (19) GB (11) 2 072 508 A

(21) Application No 8105672
(22) Date of filing 23 Feb 1981
(30) Priority data
(31) 55/024544
(32) 27 Feb 1980
(33) Japan (JP)
(43) Application published 7 Oct 1981
(51) INT CL^3 A01N 31/08
(52) Domestic classification A5E 202 247 248 252 256 257 258 269 273 279 500 501 505 508 511 512 A
(56) Documents cited GB 1058701
(58) Field of search A5E
(71) Applicant
Maruzen Oil Co Ltd
No 3
Nagahoribashisuji
1-chome
Minami-ku
Osaka-shi
Osaka
Japan
(72) Inventors
Shoichiro Watanabe
Tsuyoshi Uchibori
Hiroshi Suzuki
Kiyoshi Terada
(74) Agents
Marks & Clerk
Alpha Tower
ATV Centre
Birmingham B1 1TT

(54) An antifungal and antibacterial agent

(57) An antifungal and antibacterial agent includes poly(p-hydroxystyrene), a derivative of said poly(p-hydroxystyrene), or a salt thereof as an effective ingredient. A preferred effective ingredient is a polymer having a polymeric unit represented by the formula (I)



(I)

wherein X and X′ are each hydrogen, halogen, or $-SO_3H$, Y is hydrogen, residue of an alcohol except for the $-OH$ group, or residue of an organic or inorganic acid except for the $-OH$ group, or a salt thereof. The agent may be incorporated in such materials as wood, pulp, white water from pulp-making machines, bamboo, rush, polymers, water-soluble metal working and quenching oils and water-soluble hydraulic fluid, paint, adhesive, glue, starch, sizing agents, hides, leather, food, medicine and cosmetics.

BEST AVAILABLE COPY

GB 2 072 508 A

Certain of the chemical/mathematical formula(e) appearing in the printed specification was/were submitted in formal form after the date of filing.

SPECIFICATION

An antifungal and antibacterial agent

This invention relates to an antifungal and anti-bacterial agent.

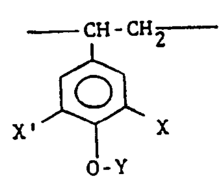
Fungi and bacteria present particular problems in humid environments. They attack many things, such as foods, medicines, wood, pulp, bamboo, rush, polymeric chemical products (e.g., plastics), oils including water-soluble metal working oils (e.g., water soluble cutting oil and water soluble rolling oil), water soluble quenching oil, and water soluble hydraulic fluid, aqueous paints, adhesive, glue, starch, hides and leather, cosmetics and sizing agents. Historically, most fungicides and bacteriocides were made of phenyl mercury, organic tin compounds, and pentachlorophenol, but since these compounds have been found to cause severe secondary pollution, their use has been largely banned. More recently, sulfur- or nitrogen-containing compounds and heterocyclic compounds have been used, but have not been found to exhibit particularly good effects. Current criteria for bacteriocides and fungicides require that they have no toxicity and cause no secondary pollution when discharged to the environments. No product fully satisfying these criteria has been available in the market. The properties common to most commercially available fungicides and bacteriocides are that they be made of compounds of low molecular weight and that they be water-soluble, but unfortunately, such properties accentuate the problem of secondary pollution.

Some phenols of low molecular weight are known to have antibacterial effects. Compounds having a slightly higher molecular weight prepared by condensing phenols with aldehydes such as formaldehyde or ketones are also known, but their antifungal and antibacterial effects are substantially lost when more than three phenol nuclei are condensed with the aldehyde or ketone. For instance, almost no antifungal or antibacterial effect is exhibited by 1-(p-hydroxyphenyl)-1-(o-hydroxy-m-ethylphenyl)-ethane.

An object of the present invention is therefore to provide an antifungal and antibacterial agent which alleviates or overcomes the above-mentioned problems experienced in the prior art.

Accordingly, the invention resides in an antifungal and antibacterial agent including as an effective ingredient poly(p-hydroxystyrene), a derivative of said poly(p-hydroxystyrene), or a salt thereof, each having a molecular weight of at least about 1500.

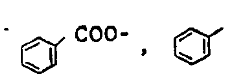
The antifungal and antibacterial agent of this invention may comprise as an effective agent poly(p-hydroxystyrene) per se, a poly(p-hydroxystyrene) wherein the nucleus is substituted by halogen or sulfonic acid groups, or wherein the phenolic hydroxyl group of which is etherized or esterified, or salts thereof. Therefore, the anti-fungal and antibacterial agent of this invention includes as an effective ingredient poly(p-hydroxystyrene) or a derivative of said poly(p-hydroxystyrene) which has a polymeric unit represented by formula (I)



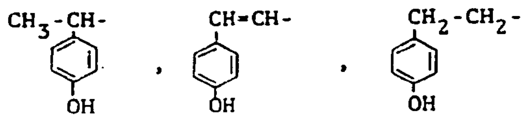
(I)

wherein X and X' are each hydrogen, halogen or $-SO_3H$, Y is hydrogen, residue of an alcohol except for the $-OH$ group or residue of an organic or inorganic acid except for the $-OH$ group, or a salt thereof, each having a molecular weight of at least about 1500.

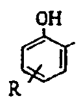
The end group of the polymer used in this invention is not extremely important. The end group of the polymer varies with the polymerization reaction (radical and cation polymerizations), polymerization initiator, reaction solvent and the like. Examples of the end group of the polymer used in this invention include

 , CH_3COO-, CH_3-, $(CH_3)_3CO-$ groups,

which are derived from a radical polymerization initiator (e.g., benzoyl peroxide, acetoyl peroxide, tert-butyl hydroperoxide),

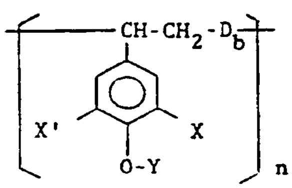
 groups,

which are derived from p-hydroxystyrene as a monomer, a residue of a solvent except for the hydrogen atom (e.g.,

RO- and 

groups, wherein R is hydrogen or an alkyl group having 1 to 10 carbon atoms, etc.) which is derived from a reaction solvent.

The polymer may be a homopolymer or a copolymer, which may be a linear copolymer or graft copolymer or may have a crosslinked three-dimensional network structure. The antifungal and antibacterial agent of this invention may be represented by the formula (I')



(I')

wherein X, X' and Y are the same as defined above, b is 0 or a positive number, D is a comonomer, and n is the degree of polymerization) or a salt thereof. In the formula (I'), n is more than about 12, preferably more than about 16. The reason b or n is not defined to be an integer is that a polymer is intrinsically a mixture and that it is better understood by defining its average structure rather than the individual constituent molecules.

The halogens X and X' in formulae (I) and (I') can include bromine, iodine, chlorine, and fluorine. Examples of Y include hydrogen; residue of an alcohol except for the –OH group such as an alkyl group, an aromatic substituted alkyl group, $-(R_1O)_mH$ group, wherein R_1 is an alkylene group having two or more carbon atoms, and m is an integer of at least one; and residue of an organic or inorganic acid except for the –OH group such as

$-\overset{\displaystyle O}{\overset{\|}{C}}-R_2$ group,

wherein R_2 is hydrogen, an alkyl group, a halogen-substituted alkyl group, an aromatic group, $-(CH_2)_pCOOH$ group, wherein p is 0 or an integer of at least one,

$-\overset{\displaystyle O}{\overset{\|}{P}}(OH)_2$,

$-\overset{\displaystyle S}{\overset{\|}{P}}(OH)_2$,

$$-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-OH \text{ and}$$

$$-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-R_3 \text{ groups,}$$

wherein R_3 is an aromatic group. The alkyl group as Y preferably has from 1 to 9, and particularly preferably from 1 to 3, carbon atoms, and examples of the alkyl group include methyl, ethyl, propyl, butyl, pentyl, hexyl and octyl. The aromatic-substituted alkyl group as Y preferably has from 7 to 10 carbon atoms, and examples of the aromatic-substituted alkyl group include benzyl, 2-phenylethyl, and 3-phenylpropyl. The oxyalkylene group R_1O preferably has from 2 to 4 carbon atoms, and examples thereof include oxyethylene, oxypropylene, and oxybutylene. The symbol m is preferably from 1 to 20, and particularly preferably from 1 to 10. The alkyl group and halogen substituted alkyl group as R_2 preferably have from 1 to 17, and particularly preferably from 1 to 4 carbon atoms, and examples of which include methyl, ethyl, propyl, trichloromethyl, monochloromethyl, butyl, pentyl, hexyl, octyl, nonyl, decyl, and dodecyl. The aromatic group as R_2 preferably has from 6 to 8 carbon atoms, and examples of which are phenyl, tolyl, and xylyl. The symbol p is preferably 0 or 1 to 8, particularly preferably 0 or 1 to 4. The aromatic group as R_3 preferably has from 6 to 10 carbon atoms, and examples there of include phenyl, tolyl, xylyl, propylphenyl and butylphenyl. The comonomer used for D according to formula (I') may be any compound, provided that the polymer contains at least about 30 wt% of the hydroxystyrene unit. When X and/or X' are $-SO_3H$ and Y is hydrogen,

$$-(R_1O)_mH,\ -CO(CH_2-)_{p}COOH,$$

$$-\overset{\overset{O}{\|}}{P}\begin{matrix}\diagup OH \\ \diagdown OH\end{matrix}\ ,$$

$$-\overset{\overset{S}{\|}}{P}\begin{matrix}\diagup OH \\ \diagdown OH\end{matrix}\ ,$$

or

$$-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-OH, \text{ the}$$

polymer contains active hydrogen, and reacts with an alkaline substance to form a salt, and the resulting salt also has antifungal and antibacterial effects. Examples of the alkaline substance that reacts with the polymer to form a salt include alkali metal hydroxides and alkaline earth metal hydroxides, such as sodium hydroxide, potassium hydroxide, lithium hydroxide, calcium hydroxide, magnesium hydroxide and barium hydroxide, and ammonia water. The polymer according to this invention, that is, poly(p-hydroxystyrene), its derivative or a salt thereof has a weight average molecular weight of at least about 1500, and preferably from about 2,000 to 5,000,000. A polymer having too low a molecular weight is volatile and unsuitable for use as an active ingredient of the antifungal and antibacterial agent of this invention.

The polymer described above can be prepared by known methods generally used in the reactions of phenols. Examples of the method or preparing p-hydroxystyrene polymers are described in Japanese Patent Application (OPI) Nos. 13694/78 (the term "OPI" as used herein means an unexamined published Japenese patent application), 109097/76, 52594/78,

22187/73, 23193/77, 58087/77, and 105389/76. Poly(p-hydroxystyrene) can be prepared by cationic, radical or thermal polymerization of p-hydroxystyrene, and polymers having a weight average molecular weight of from several hundred to about 350,000 can be easily prepared by properly selecting the polymerization conditions. A polymer having a molecular weight greater than 350,000 can be produced by radical polymerization of p-methoxystyrene or p-acyloxystyrene such as p-acetoxystyrene, followed by hydrolysis with acid or alkali. The p-hydroxystyrene polymer used in this invention may be a copolymer of p-hydroxystyrene, p-methoxystyrene or p-acyloxystyrene with another vinyl monomer. Such copolymer can be produced by radical or cationic polymerization. Examples of the comonomer that can be copolymerized with p-hydroxystyrene, p-methoxystyrene or p-acyloxystyrene include styrene, acrylonitrile, maleic anhydride, acrylic acid, methacrylic acid, acrylamide, acrylic ester, and methacrylic ester. A polymer having a cross-linked three-dimensional network structure can be prepared by copolymerizing p-hydroxystyrene, p-methoxystyrene or p-acyloxystyrene with a polyene compound such as divinylbenzene, butadiene, isoprene, cyclopentadiene, diol ester of acrylic acid, diol ester of methacrylic acid and ethylidene norbornene.

Polymers wherein p-acyloxystyrene or p-hydroxystyrene is grafed onto a hydrocarbon polymer can be produced by irradiating a hydrocarbon polymer such as polyethylene, polypropylene or polystyrene with ionizing radiation, followed by immersing the irradiated polymer in a solution containing p-acyloxystyrene or p-hydroxystyrene. The graft type polymers are described in Japanese Patent Publication Nos. 31234/77 and 31235/77.

The nucleus of the p-hydroxystyrene polymer can be substituted by a halogen by a known method, for instance, the method described in Japanese Patent Publication No. 33680/77. A p-hydroxystyrene polymer the nucleus of which is sulfonated is described in, say, Japanese Patent Application (OPI) No. 109097/76 according to which, a p-hydroxystyrene polymer is dissolved in a solvent such as acetic acid and treated with a sulfonating agent such as sulfuric anhydride at from 20°C to 60°C.

An ether of p-hydroxystyrene polymer wherein Y is methyl can be readily obtained by treating a solution of the polymer in a solvent (e.g., tetrahydrofuran) with diazomethane at room temperature. An ether of p-hydroxystyrene polymer wherein Y is alkyl or aromatic substituted alkyl is prepared by first treating a solution of the polymer in a solvent (e.g., dioxane) with aqueous sodium hydroxide to form a salt wherein Y is Na and then by reacting the salt with a halogenated hydrocarbon such as alkyl iodide, alkyl bromide, or benzyl iodide at 50°C to 150°C (the Williamson process). An ether of p-hydroxystyrene polymer wherein Y is $-R_1O)_mH$ can be obtained by treating a solution of the polymer in a solvent (e.g., dioxane) with an alkylene oxide (e.g., ethylene oxide, propylene oxide, or butylene oxide) in the presence of an alkali catalyst at from 50°C to 150°C.

An ester of p-hydroxystyrene polymer wherein Y is

$$-\overset{\overset{\displaystyle O}{\|}}{C}-R_2$$

can be obtained by first treating a solution of the polymer in a solvent (e.g., dioxane) with sodium hydroxide to form a salt wherein Y is Na and then by reacting the salt with an acid anhydride or acid chloride of mono- or dicarboxylic acid at from 0°C to 150°C. Examples of the carboxylic acid include formic acid, acetic acid, trichloroactic acid, propionic acid, butyric acid, pivalic acid, stearic acid, lauric acid, oxalic acid, malonic acid, succinic acid, glutaric acid, adipic acid, sebacic acid, benzoic acid, and phthalic acid. Derivatives of a poly(p-hydroxystyrene) wherein Y is

$$-\overset{\overset{\displaystyle O}{\|}}{P}\begin{matrix}\diagup OH\\ \diagdown OH\end{matrix}$$

or

$$-\overset{\overset{\displaystyle S}{\|}}{P}\begin{matrix}\diagup OH\\ \diagdown OH\end{matrix}$$

are described in Japanese Patent Application (OPI) No. 52594/78. A derivative of poly(p-

hydroxystyrene) wherein Y is

$$-\overset{\overset{\large O}{\|}}{\underset{\underset{\large O}{\|}}{S}}-OH$$

can be prepared by treating a solution of the polymer in a solvent (e.g., dioxane) with aqueous sodium hydroxide to form a sodium salt which is then treated with chlorosulfonic acid at from 0°C to 100°C. An ester of poly(p-hydroxystyrene) wherein Y is

$$-\overset{\overset{\large O}{\|}}{\underset{\underset{\large O}{\|}}{S}}-R_3$$

can be prepared by treating a solution of the polymer in a solvent (e.g., tetrahydrofuran) with sodium hydroxide to form a salt wherein Y is Na and then by reacting the salt with an acid chloride of aryl sulfonic acid such as benzenesulfonyl chloride or p-toluenesulfonyl chloride at from 0°C to 150°C. As described above, these polymers react with an alkaline substance to form a salt when X, X', or Y contain active hydrogen. The method of forming the salt is described in Japanese Patent Application (OPI) No. 52594/78, etc.

Typical examples of poly(p-hydroxystyrene), its derivatives and salts thereof are identified in Table 1 below. The structure of these polymers was identified by IR and NMR spectrum analysis, and their weight average molecular weights were determined by gel-permeation chromatography.

Table 1

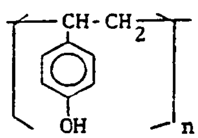
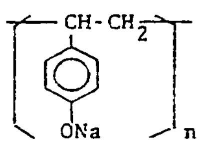
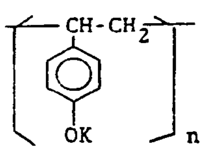
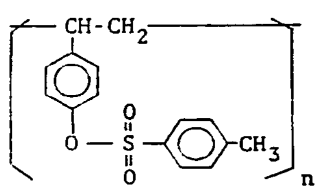
Comp. No.	Structural Formula	Molecular Weight (Mw)	Elemental Analysis - Wt% Found (Calculated)	IR Adsorption Frequency (cm^{-1})
No. 1		4,000	C: 79.8 (80.0) H: 6.61 (6.67)	3400S 1520S 1240S 830S
No. 2		4,500	C: 68.5 (67.6) H: 4.88 (4.93) Na: 16.0 (16.2)	
No. 3		5,000	K: 24.8 (24.7)	
No. 4		8,200	C: 65.1 (65.7) H: 5.02 (5.11) S: 11.2 (11.7)	1510S 1180S 830S

Table 1 (continued)

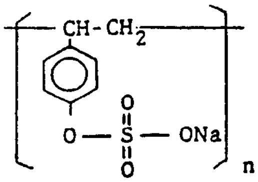
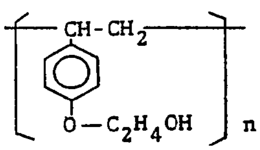
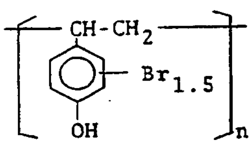
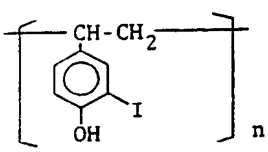
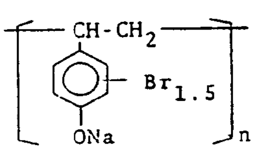
No. 5		6,100	C: 42.8 (43.2) H: 3.11 (3.15) S: 13.9 (14.4) Na:10.5 (10.4)	1500M 1240S 830M
No. 6		5,000	C: 73.6 (73.2) H: 7.16 (7.32)	3400S 1500S 1220S 830M
No. 7		7,400	C: 39.6 (40.3) H: 2.65 (2.73) Br:50.0 (50.3)	3500S 1480S 1160S 870M 740S
No. 8		7,900	C: 39.9 (39.0) H: 2.91 (2.85) I: 51.9 (51.6)	3500S 1490S 820M 730S
No. 9		8,300	Br:46.4 (46.1) Na:8.80 (8.83)	

Table 1 (continued)

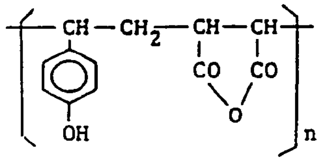
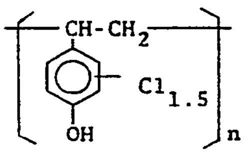
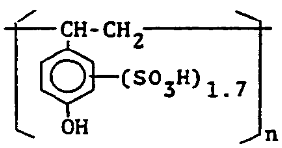
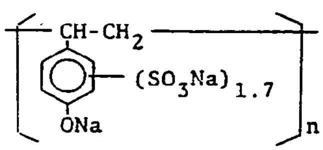
No.10		9,500	C: 65.1 (66.1) H: 4.62 (4.59)	3450S 1780S 1520S 1220S 830M
No.11	Polyethylene on which p-hydroxystyrene is grafted	1×10^6	C: 81.8 (81.1) H: 8.00 (8.11)	3400S 1520S 1240S 830S 720S
No.12		2,300	C: 55.8 (55.9) H: 3.61 (3.78) Cl:30.2 (31.0)	3500S 1480S 1100S 850M 760S
No.13		3,400	C: 38.2 (37.5) H: 3.06 (3.13) S: 21.5 (21.3)	3330S 1450S 1150S 810M
No.14		4,100	S: 16.7 (17.2) Na:19.8 (19.7)	

Table 1 (continued)

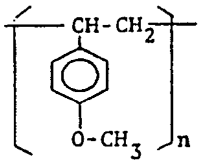
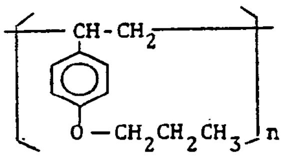
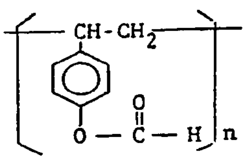
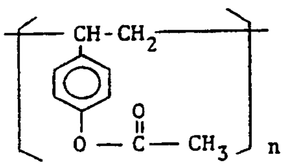
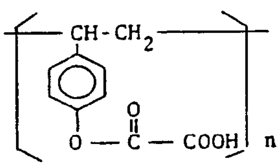
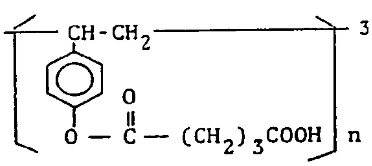
No.15		1,900	C: 80.4 (80.6) H: 7.38 (7.46)	1510S 1240S 830M
No.16		2,200	C: 81.7 (81.5) H: 8.83 (8.64)	1510S 1240S 830M
No.17		1,800	C: 71.9 (73.0) H: 5.52 (5.41)	1750S 1500M 1240S 830S
No.18		2,000	C: 73.6 (74.1) H: 6.22 (6.17)	1750S 1500M 1240S 830S
No.19		2,500	C: 62.9 (62.5) H: 4.06 (4.17)	1750S 1710M 1510M 1220M 840M
No.20		3,000	C: 65.9 (66.7) H: 6.04 (5.98)	1750S 1710M 1510S 1220M 830M

Table 1 (continued)

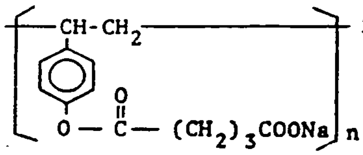
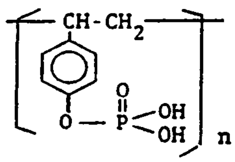
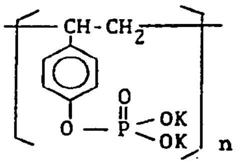
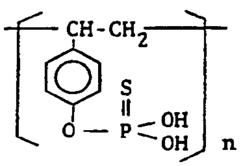
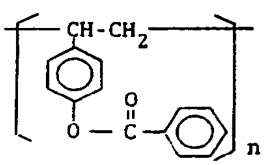
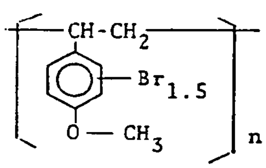
No.21		3,200	Na:8.96 (8.98)	
No.22		6,500	C: 48.7 (48.0) H: 4.44 (4.50) P: 15.1 (15.5)	3400S 1510M 1220S 970S 830M
No.23		9,000	P: 11.0 (11.2) K: 28.2 (28.3)	
No.24		6,800	C: 43.2 (44.4) H: 4.14 (4.17) P: 13.9 (14.4) S: 13.7 (14.8)	3400S 1520S 1240S 970W 830S
No.25		7,000	C: 80.0 (80.4) H: 5.41 (5.36)	1730S 1510M 1200M 830M
No.26		16,000	C: 42.1 (42.8) H: 3.29 (3.37) Br:48.1 (47.5)	1480S 1160S 870M 740S

Table 1 (continued)

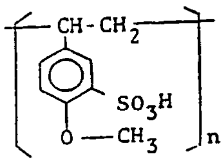
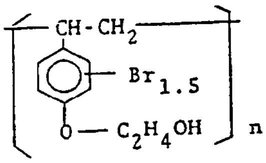
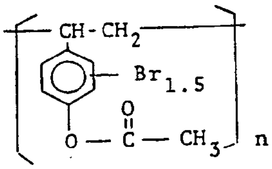
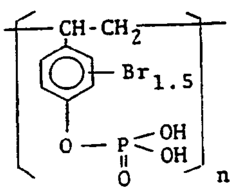
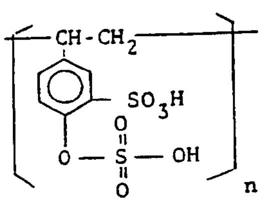
No.27 	14,000	C: 49.8 (50.5) H: 4.73 (4.67) S: 14.5 (15.0)	3400S 1500S 1240S 1160S 830M
No.28 	18,000	C: 42.5 (42.5) H: 3.88 (3.72) Br: 41.7 (42.5)	3400S 1480S 1220S 870M 740M
No.29 	18,000	C: 41.9 (42.8) H: 2.99 (3.03) Br: 42.0 (42.8)	1750S 1480S 1160S 870M 740S
No.30 	21,000	C: 30.6 (30.1) H: 2.41 (2.35) Br: 37.9 (37.7) P: 9.61 (9.73)	3400S 1500S 1210S 830M 740S
No.31 	13,000	C: 33.3 (34.3) H: 2.84 (2.86) S: 20.9 (22.9)	3400S 1515M 1170S 830M

Table 1 (continued)

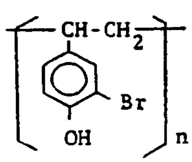
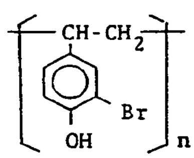
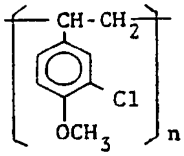
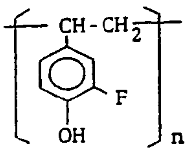
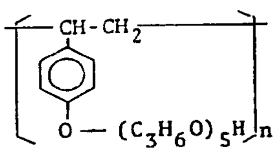
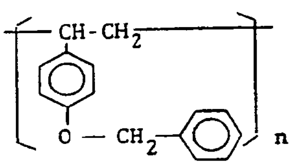
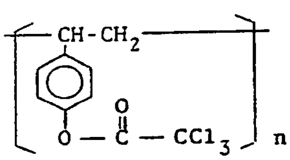
No.32	Copolymer of p-hydroxystyrene and styrene (mol. ratio=0.70:0.30)	6,500	C: 85.1 (83.3) H: 7.17 (6.94)	3400S 1520S 1240S 830S
No.33	Copolymer of p-hydroxystyrene and acrylonitrile (mol. ratio=0.66:0.34)	7,300	C: 77.1 (77.8) H: 6.53 (6.48) N: 4.84 (4.90)	3400S 2230M 1510S 1215S 830S
No.34	Copolymer of p-hydroxystyrene and acrylic acid (mol. ratio=0.65:0.35)	6,000	C: 71.6 (72.7) H: 6.33 (6.40)	3400S 1710S 1520S 1240S 830S
No.35	Copolymer of p-acetoxystyrene and divinylbenzen (mol. ratio=0.80:0.20)	$>1 \times 10^4$	C: 79.4 (77.1) H: 6.61 (6.43)	1750S 1500M 1240S 830S
No.36	Copolymer of p-acetoxystyrene and butadiene (mol. ratio=0.83:0.17)	$>1 \times 10^4$	C: 77.2 (75.0) H: 6.68 (6.49)	1750S 1510M 1240S 840S
No.37		2.3×10^5	C: 47.7 (48.2) H: 3.46 (3.52) Br:40.0 (40.2)	3500S 1500S 1180S 820S 740M
No.38		4.5×10^6	C: 48.5 (48.2) H: 3.64 (3.52) Br:39.8 (40.2)	3500S 1500S 1180S 830S 740M

Table (continued)

No.39		2.0×10^5	C: 64.5 (64.1) H: 5.38 (5.34) Cl: 20.7 (21.1)	1480S 1240S 850M 760S
No.40		4,500	C: 70.1 (69.6) H: 5.01 (5.07) F: 13.0 (13.8)	3500S 1500S 1200S 820M 770S
No.41		12,500	C: 66.8 (67.3) H: 9.26 (9.27)	3400S 1500S 1100S 820M
No.42		7,000	C: 85.3 (85.7) H: 6.66 (6.63)	1500S 1200M 1100S 820M
No.43		8,600	C: 44.9 (45.2) H: 2.70 (2.64) Cl: 39.7 (40.1)	1750S 1510M 1240S 830M

Notes: (1) The symbol n represents the degree of polymerization.

(2) The nuclear substituent in compounds Nos. 7, 9, 12, 13, 14, 26, 28, 29 and 30 was in orthoposition with respect to the hydroxy or substituted-hydroxy group.

(3) Compound No. 11 was prepared by grafting 100% p-acetoxystyrene onto a polyethylene film (200 microns thick) obtained by low pressure polymerization process by means of irradiation with ionizing radiation, followed by hydrolysis of the acetoxy group.

(4) IR absorption frequency refers to characteristic absorptions, with S, M and W representing strong, medium and weak absorptions, respectively.

The poly(p-hydroxystyrene), its derivatives and salts thereof contained as effective ingredients in the antifungal and antibacterial agent of this invention are incorporated in materials in which they are used either directly or after being dispersed in a carrier or dissolved in a solvent. Conventional methods of incorporation can be used, including coating, spraying, kneading, immersion and hot spraying. The polymer can be incorporated in liquids simply by mixing. Examples of the material to which the antifungal and antibacterial agent according to this invention can be applied include wood, pulp, white water from paper making machines, bamboo, rush, polymeric substances such as plastics, water-soluble metal working oil, water-soluble hydraulic fluid, water-soluble quenching oil, paints, adhesives, glue, starch, sizing agent, hides and leather, foods, medicines, and cosmetics. The antifungal and antibacterial agent is generally incorporated in these materials in such an amount that the polymer constituting the effective ingredient is present at a concentration of from about 0.5 to 10,000 ppm (by weight).

The poly(p-hydroxystyrene), its derivatives or salts thereof used in this invention are unique in that unlike conventional antifungal and antibacterial agents, they exhibit antibacterial and antifungal effect without volatilizing and present little or no toxicity to the human body. A group of mice administered poly(p-hydroxystyrene) did not change greatly in their general conditions and their internal organs did not exhibit any abnormal conditions when it was administered orally in a single dose (1000 mg/kg), or in divided portions (500 mg/kg × 7 for 14 days, i.e., 500 mg/kg per two days × 7), or administered subcutaneously (10 g/kg). Another group of mice administered a derivative of poly(p-hydroxystyrene) wherein the nucleus was brominated did not change greatly in their general conditions or their internal organs did not exhibit any abnormal conditions, when it was administered orally in divided portions (500 mg/kg per day for 15 days). Because of this low toxicity, it is practically impossible for animals to be administered a lethal dose of the polymer according to this invention.

The poly(p-hydroxystyrene), its derivatives and salts thereof do not sublime, and they are free from blooming or bleeding in which their vapor crystallizes and condenses in a closed container or migrates to the surface of a material in which they are incorporated. Therefore, they do not cause any harm to a lens, shutter, and other parts in precision instruments such as a camera or microscope. Since they have virtually no vapor pressure and do not sublime, they can be used with advantage for preventing the growth of fungi on films that need extended storage. Paint, wall paper and synthetic leather containing the polymer according to this invention are protected from mold attack, and wood impregnated therewith is protected against fungal growth. Other characteristics of the poly(p-hydroxystyrene), its derivatives and salts thereof are: they do not reduce electrical properties (i.e., dielectric breakdown resistance (BDV), and volume resistance (IR)); they do not corrode metals; they do not impair the appearance or characteristics of natural or synthetic fibers, hides and leather, and paper. Because of these advantages, the polymer according to this invention can find numerous uses.

This invention is now described in greater detail by reference to the following examples and comparative example, which are provided here for illustrative purposes only, and are not intended to limit the scope of the invention.

Example 1

Compounds Nos. 1 to 11 noted in Table 1 were diluted in ethanol, and 1 ml of each ethanol dilution was injected into plate culture media having the final concentrations of 1000 μg/ml, 500 μg/ml, 250 μg/ml, 100 μg/ml, 50 μg/ml, 25 μg/ml and 10 μg/ml. Test microorganisms were transplanted to the media, where bacteria were cultured at 37°C for 48 hours, and fungi at 25°C for 7 days, for determination of the minimum inhibitory concentration (MIC) (in μg/ml) of each compound. The media for cultivation of bacteria consisting of a common agar culture medium of Eiken-sha, Japan (0.05 g of meat extract, 0.1 g of peptone, 0.05 g of sodium chloride, 0.15 g of agar, and 10 ml of purified water, pH = 7). Those for cultivation of fungi consisted of Sabouraud culture medium (0.3 g of glucose, 0.1 g of peptone, 0.15 g of agar, and 10 ml of purified water, pH = 6.5). The results are shown in Table 2 below.

Table 2

Microoganism	Compound										
	No. 1	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7	No. 8	No. 9	No. 10	No. 11
Staphylococcus aureus 209 PJC-1	250	500	500	250	250	250	50	50	50	500	500
Bacillus subtilis PCI-219	250	500	500	250	250	250	250	250	100	250	500
Sarcina lutea ATCC-1001	500	500	500	500	1000	250	100	250	500	100	100
Escherichia coli NIHJ	10	25	25	100	100	10	10	25	25	50	100
Salmonella typhi H-901W	25	50	100	100	100	25	25	50	50	25	100
Pseudomonas Aeruginosa IFO-3080	25	50	50	25	50	25	50	50	50	50	100
Candida albicans ATCC-7491	250	250	100	250	250	100	250	100	250	250	500
Saccharomyces cerevisiae	250	250	250	500	500	500	250	250	250	250	500
Trichophyton interdigital	10	25	25	100	100	100	10	10	50	25	100
Microsporium gypseum	10	10	25	100	100	25	25	50	25	10	50
Penicillium chrysogenum	50	100	100	50	100	25	100	100	250	100	250
Aspergillus niger ATCC-6275	50	50	50	100	50	50	50	50	50	100	50

Example 2

Mice were administered orally with a single dose of compound Nos. 1 to 11 of this invention for determination of the lethal dose LD50. The results are shown in Table 3 below.

Table 3

Sample	Lethal Dose LD50 (g/kg)
No. 1	>15
No. 2	>15
No. 3	>15
No. 4	10
No. 5	>15
No. 6	10
No. 7	1
No. 8	2
No. 9	2
No. 10	10
No. 11	>15

Example 3

The procedure of Example 1 was repeated using compound Nos. 12 to 43 of this invention for determination of their MIC. The test microorganisms were Escherichia coli NIHJ, Penicillium chrysogenum and Asperigillus niger ATCC-6275, and each compound was used in concentrations of 50, 100 and 250 μg/ml. The results are shown in Table 4.

Example 4

Mice were administered orally in single doses of 0.5 g/kg, 2 g/kg, and 5 g/kg, compound Nos. 12 to 43 in the same manner as in Example 2. The lethal doses LD50 of the respective compounds are shown in Table 4.

Table 4

Sample	MIC (μg/ml) E.C.	P.C.	A.N.	Lethal Dose, LD50 (g/kg)
No. 12	50		50	5
No. 13	50		100	>5
No. 14	50		50	>5
No. 15	50	50		5
No. 16	50	50		5
No. 17	50	100		5
No. 18	50		100	>5
No. 19	100		100	>5
No. 20	50		100	>5
No. 21	100	250		>5
No. 22	50	50		2
No. 23	50	50		2
No. 24	50	50		2
No. 25	50	100		>5
No. 26	50	50		0.5
No. 27	100		100	>5
No. 28	50		50	2
No. 29	50		50	2
No. 30	50		50	0.5
No. 31	50		100	>5
No. 32	250	250		>5
No. 33	50	100		>5
No. 34	100	250		>5
No. 35	50	100		>5
No. 36	50	100		>5
No. 37	50		50	2
No. 38	50		50	5
No. 39	50		50	2
No. 40	100		50	5
No. 41	100	250		>5
No. 42	50	50		5
No. 43	50	50		5

Notes: E.C.: Escherichia coli NIHJ
P.C.: Penicillium chrysogenum
A.N.: Aspergillus niger ATCC-6275
The absence of MIC values means that the samples were not tested.

Comparative Example 1

For comparison, the MIC of a phenolic novolak resin (m.w. = 500) prepared by reacting p-cresol and formaldehyde in the presence of an acid catalyst was determined to be 1500 μg/ml against Escherichia coli NIHJ and 2000 μg/ml against Asperigillus niger ATCC-6275.

Example 5

A test was conducted to determine the effectiveness of the antifungal and antibacterial agent of this invention when it was applied to walls: a mixture of 500 ppm of compound No. 1 with an acrylic emulsion paint (composed of 15% polyacrylate, 5.4% rutile titanium dioxide, 12% aluminum silicate, 50% water, and the balance thickener, dispersant, and defoaming agent) was applied to a test piece and left to stand at 35°C and 80% relative humidity. Even after 6 months, no mold grew on the treated surface of the test piece. No mold grew on the surface of a test piece which was treated with compound No. 7 in the same manner. When a test piece was treated with the acrylic emulsion paint that did not contain the effective ingredient of this invention, mold appeared on the treated surface after one month.

Example 6

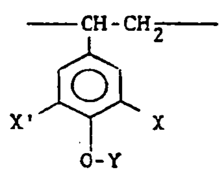
To a sample of white water from the paper making machine in a paper mill, 250 ppm of compound No. 1 of this invention was added, and the mixture was held at 35°C. Little fungal growth (a few colonies/ml) was observed even after 5 days of storage. The same test was

conducted with compound No. 7 and little fungal growth was observed. However, when the white water did not contain the effective ingredient of this invention, much mold (1×10^8 colonies/ml) appeared in only 2 days.

CLAIMS

1. An antifungal and antibacterial agent including as an effective ingredient poly(p-hydroxystyrene), a derivative of said poly(p-hydroxystyrene), or a salt thereof, each having a molecular weight of at least about 1500.

2. An antifungal and antibacterial agent according to Claim 1 wherein the effective ingredient is a poly(p-hydroxystyrene) or its derivative, each comprising at least 12 polymeric units represented by formula (I)



(I)

wherein X and X' are each hydrogen, halogen, or $-SO_3H$, Y is hydrogen, residue of an alcohol except for the $-OH$ group, or residue of an organic or inorganic acid except for the $-OH$ group, or a salt thereof.

3. An antifungal and antibacterial agent according to Claim 2 wherein Y is: hydrogen; an alkyl group; and aromatic substituted alkyl group; $-(R_1O)_mH$, wherein R_1 is an alkylene group having two or more carbon atoms, and m is an integer of at least 1; and

$$-\overset{\displaystyle O}{\overset{\|}{C}}-R_2,$$

wherein R_2 is hydrogen, an alkyl group, a halogen substituted alkyl group, an aromatic group, or $-(CH_2)_pCOOH$, wherein p is 0 or an integer of at least 1;

$$-\overset{\displaystyle O}{\overset{\|}{P}}(OH)_2 \quad ;$$

$$-\overset{\displaystyle S}{\overset{\|}{P}}(OH)_2 \quad ;$$

$$-\underset{\underset{\displaystyle O}{\|}}{\overset{\overset{\displaystyle O}{\|}}{S}}-OH;$$

or

$$-\underset{\underset{\displaystyle O}{\|}}{\overset{\overset{\displaystyle O}{\|}}{S}}-R_3,$$

wherein R_3 is an aromatic group,

4. An antifungal and antibacterial agent according to Claim 2 or 3 wherein the poly(p-hydroxystyrene), or derivative thereof is a copolymer of p-hydroxystyrene or a derivative thereof and another vinyl monomer.

5. An antifungal and antibacterial agent according to Claim 2 or 3 wherein the p-hydroxystyrene, its derivative, or a salt thereof comprises at least 16 polymeric units represented by formula (I).

6. An antifungal and antibacterial agent according to Claim 2 or 3 wherein the poly(p-hydroxystyrene), its derivative, or a salt thereof has a molecular weight of from 2,000 to 5,000,000.

7. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is poly(p-hydroxystyrene).

8. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is an alkali metal salt of poly(p-hydroxystyrene).

9. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is poly(p-hydroxystyrene) halogenated at at least one position ortho- to the hydroxy group.

10. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is an alkali metal salt of poly(p-hydroxystyrene) halogenated at at least one position ortho- to the hydroxy group.

11. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is a copolymer of p-hydroxystyrene and maleic anhydride.

12. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is polyethylene on which p-hydroxystyrene is grafted.

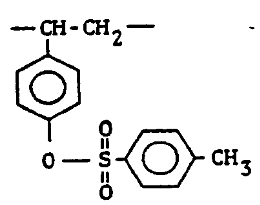
13. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is poly(p-alkoxystyrene).

14. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is poly(p-acyloxystyrene).

15. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is poly(p-hydroxystyrene) sulfonated at at least one position ortho- to the hydroxy group.

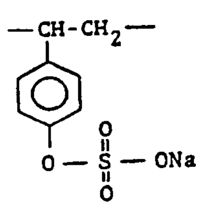
16. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is an alkali metal salt of poly(p-hydroxystyrene) sulfonated at at least one position ortho- to the hydroxy group.

17. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is a polymer having a repeating unit of formula (II)



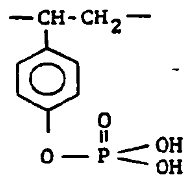
(II)

18. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is a polymer having a repeating unit of formula (III)



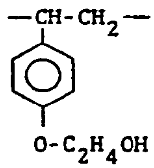
(III)

19. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is a polymer having a repeating unit of formula (IV)



(IV)

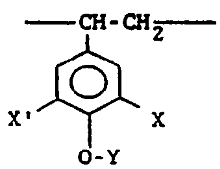
20. An antifungal and antibacterial agent according to Claim 2 wherein the effective ingredient is a polymer having a repeating unit of formula (V)



(V)

21. A material containing an antifungal and antibacterial agent including as an effective ingredient poly(p-hydroxystyrene), a derivative of said poly(p-hydroxystyrene), or a salt thereof, each having a molecular weight of at least about 1500.

22. A material as in Claim 21 wherein the effective ingredient is a poly(p-hydroxystyrene) or its derivative, each comprising at least 12 polymeric units represented by formula (I)



(I)

wherein X and X′ are each hydrogen, halogen, or $-SO_3H$, Y is hydrogen, residue of an alcohol except for the $-OH$ group, or residue of an organic or inorganic acids except for the $-OH$ group, or a salt thereof.

23. A material as in Claim 22 wherein Y is: hydrogen; an alkyl group; an aromatic substituted alkyl group; $-(R_1O)_mH$, wherein R_1 is an alkylene group having two or more carbon atoms, and m is an integer of at least 1; and

$$-\overset{\displaystyle O}{\overset{\|}{C}}-R_2,$$

wherein R_2 is hydrogen, an alkyl group, a halogen substituted alkyl group, an aromatic group, or $-(CH_2)_pCOOH$, wherein p is 0 or an integer of at least 1;

$$-\overset{\displaystyle O}{\overset{\|}{P}}\!\begin{array}{l}\diagup OH\\ \diagdown OH\end{array} \quad ;$$

$$-\overset{\displaystyle S}{\overset{\|}{P}}\!\begin{array}{l}\diagup OH\\ \diagdown OH\end{array} \quad ;$$

$$-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}-OH;$$

or

$$-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}-R_3$$

wherein R_3 is an aromatic group.

24. A material according to Claim 21, 22 or 23, wherein the material selected from the group consisting of wood, pulp, white water from paper making machines, bamboo, rush, polymeric substances, water-soluble metal working oil, water-soluble hydraulic fluid, water-soluble quenching oil, paint, adhesive, glue, starch, sizing agent, hides and leather, food, medicine, and a cosmetic.

25. A material as in Claim 21, 22, or 23, wherein the effective ingredient is present in a concentration of from 0.5 to 10,000 ppm.

26. A material as in Claims 21, 24, wherein the effective ingredient is present in a concentration of from 0.5 to 10,000 ppm.

27. A method of protecting a material against fungi and bacteria comprising the step of applying thereto an antifungal and antibacterial agent including as an effective ingredient poly(p-hydroxystyrene), a derivative of said poly(p-hydroxystyrene), or a salt thereof, each having a molecular weight of at least about 1500.

28. An antifungal and antibacterial agent as claimed in Claim 1 substantially as hereinbefore described.

29. A method as claimed in Claim 27 of protecting a material against fungi and bacteria substantially as hereinbefore described with reference to Example 5 or Example 6.

30. A material protected against fungi and bacteria by a method as claimed in Claim 27 or Claim 29.

Printed for Her Majesty's Stationery Office by Burgess & Son (Abingdon) Ltd.—1981.
Published at The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.